Claim 1 was objected to because the word "cell" was misspelled. The claim has been amended to correct this deficiency.

Claim 2 was rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 2 has been amended so that it no longer claims "derivatives" of the missing region. Thus, claim 2 is now believed to be allowable.

Claim 3 was amended and claim 5 has been added to claim derivatives of the missing region. These claims are limited to derivatives with "at least 70% homology to the missing region". These claims are also limited to peptide derivatives which have maintained the physiological activity of the peptides from which they were derived. Applicant now submits that "one of skill in the art would recognize that the applicant was in possession of the necessary common attributes of features of the elements possessed by the members of the [genus] in view of the species disclosed."

Claims 1- 4 were rejected under 35 U.S.C. § 112, second paragraph, as "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner felt that the phrase "examining a receptor" was confusing. Although applicant believes that the language was clear, the claims have been amended to remove this language. Applicant now submits that all claims are compliant with 35 U.S.C. § 112.

Claim 1 was rejected under 35 U.S.C. § 102(b) as being anticipated by Song et al. (Proc. Natl. Acad. Sc. I. USA., 90: 9085-9089, 1993).

Song et al. disclose two human gastrin/cholecystokinin type B (CCK_B) receptor gene variants. Song et al. also disclose that the shorter isoform of the receptor lacks a pentapeptide sequence that is present in the longer isoform and *suggests* that the pentapeptide sequence "*may be of potential functional importance*."

Song et al. do not teach any physiological activity or biological activity of the peptide, the receptor variants or receptor antagonists. Song et al. teaches only that the peptide *may* have functional importance. No disclosure nor data is presented that demonstrates physiological activity.

Additionally, Song et al. only teach a potential functional importance of the peptide in context of the entire receptor, not as a stand alone peptide. This is underscored by the following disclosure:

> Alternative splicing occurs in the third intracellular loop of certain other G protein-coupled receptors, such as the human D_2 and D_3 dopamine receptors (21-23). In the case of the D_2 and D_3 dopamine receptor, alternative splicing may affect the coupling of the receptor to second-messenger pathways (24, 25). Thus, the pentapeptide cassette in the gastrin/CCK_B receptor may be of potential functional importance.

Thus, any potential physiological importance is discussed in the context of the affect it would have on how the gastrin/CCK_B *receptor* may function or interact as other G protein-coupled receptors function.

Nor do Song et al. teach "a substance or cell present *in vivo* having a functional antagonism against the ligand for the [CCK_B] receptor or against a cell which expresses the [CCK_B] receptor of the ligand." Applicants submit that both the amendments and the arguments distinguish claim 1 and its dependent claims over the cited reference.

Claims 1-4 were also rejected under 35 U.S.C. § 103(a) as being unpatentable over Song et al. and in view of Naranda et al.

As discussed above, Song et al. do not teach any physiological activity or biological activity of the peptide, the receptor variants or receptor antagonists. Song et al. teaches only that the peptide *may* have functional importance. Additionally, Song et al. only

teach a potential functional importance of the peptide in context of the entire receptor, not as a stand alone peptide.

Naranda et al. discloses that peptides of the insulin receptor (IR) that have sequence similarity with the major histocompatibility class 1 antigen complex (MHC 1) bind to the IR receptor and inhibit receptor internalization. Thus, the bioactivity disclosed by Naranda et al. is limited to peptides with sequence homology to MHC-1, particularly as a result of its self-assembly properties. Naranda et al. on p. 11697, col. 1, states:

> One way to interpret our findings is to suppose that MHC-1 itself plays some role in receptor endocytosis by interacting with a receptor and that this interaction is competitively blocked by the bioactive peptides. The underlying principle seems to be self-assembly, *i.e.*, interaction of identical or similar sequences. The affected receptors do not share a common motif for interaction with alpha 1 sequence of MHC-1, but the latter-- like a master key-- can recognize distinctively different sequences among different receptors. We suggest that the principle and method described here may be generally applicable to identifying receptor domains that play a role in receptor endocytosis.

Thus, the only express motivation provided by Naranda et al. is identifying receptor-specific sites of importance *as evidenced by their homology to MHC-1*.

The Examiner suggests that "an ordinary practitioner would have been motivated to analyze active peptides of different sizes of the receptor, because Naranda et al. thought they may enhance sensitivity to agonists . . . " Applicants respectfully suggest that this is not the case. An ordinary practitioner would only have been motivated to analyze peptides that had significant homology to MHC-1, not any peptide sequence that may be a part of the receptor.

It is first respectfully submitted that the rejection of the claims cannot be maintained over the references, as none of the references teach or suggest the subject matter of these claims.

Applicants submit that the claims are now in condition for allowance, and respectfully request a notice to that effect. If the Examiner believes that further discussion will advance the prosecution of the application, she is highly encouraged to telephone applicant's attorney at the number given below.

A check in the amount of $200.00 is enclosed to cover the petition for two-month extension of time fee. Please charge any additional fees or credit any overpayments as a result of the filing of this paper to our Deposit Account No. 02-3978 — a duplicate of this paper is enclosed for that purpose.

Respectfully submitted,

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Date: October 24, 2001

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Attachment

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A method for [searching] the identification of physiologically active [substances] peptides, the method comprising the steps of[;]:

[examining a receptor having an amino acid sequence having two or more sizes for the same receptor by comparing a cDNA sequence of said receptor] comparing the cDNA sequences of receptor variants of receptors having one or more variants in size, the receptors being receptive of an identical ligand and being products of the same gene, wherein [the receptor being a receptor of a cell producing an antagonist to substance in a body or a receptor of a cell producing an antagonist to said dell *per se*] there is a substance or cell present in vivo having a functional antagonism against the ligand for the receptor or against the cell which expresses the receptor of the ligand; and

[examining which region of] identifying which cDNA sequence in the [longer] larger receptor [are] is missing in the shorter receptor [by comparing the sequences of the cDNAs].

2. (Amended) A method of producing physiologically active peptides, wherein the missing region determined by the method of claim 1, [or its derivatives], [are] is produced.

3. (Amended) A method of claim 2, wherein a derivative having at least 70% homology to the missing region, is produced, wherein the physiological activity of the derivative is maintained.

4. (Amended) A method of claim [3] 2, wherein the missing region is synthesized by chemical synthesis.

Applicants submit that the claims are now in condition for allowance, and respectfully request a notice to that effect. If the Examiner believes that further discussion will advance the prosecution of the application, she is highly encouraged to telephone applicant's attorney at the number given below.

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